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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,252	01/28/2005	Jef D Boeke	JHU1870-1	9085

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EXAMINER	
PETERSEN, CLARK D	

ART UNIT	PAPER NUMBER
1657	

MAIL DATE	DELIVERY MODE
06/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,252	BOEKE ET AL.	
	Examiner	Art Unit	
	Clark D. Petersen	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *21-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 1-20, in the reply filed on 16 April 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 21-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 16 April 2007.

Specification

The instant specification recites that priority extends under 35 USC 119(e) to provisional application 60/363,708; however the instant application is filed under 35 USC 371. Please update the priority information.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 depends from claim 1. Claim 1 recites "detecting altered manganese ion transport". Claim 15 recites "detecting altered magnesium transport". Claim 16 also recites "magnesium ion concentration".

Claim 17 depends from claim 1. Claim 1 recites "A method of identifying an agent that modulates reverse transcriptase activity in a cell..." Claim 17 recites "comprises detecting altered reverse transcriptase activity..." as a method step. This is redundant. Because claims 18-20 depend from 17, these claims, too, are rejected as being indefinite.

It should also be noted that as the method of claims 17-20 is currently recited, any inhibitor of reverse transcriptase activity would be interpreted by Applicants as inhibiting manganese transport, i.e. the claims teach that any change in activity would lead to the conclusion that manganese transport was being altered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 7, 10, 11, and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Wei et al (J Biol Chem, 4 Aug 2000) in light of Supek et al (PNAS, May

1996). Wei et al teach a method of studying mutants of the pmr1p calcium/manganese transporter in yeast. These yeast cells have pmr1p knocked out. Because yeast normally also express the SMF1 manganese transporter (see Supek et al, Abstract, for example), these yeast still read upon a cell expressing a divalent cation transporter, as required in instant claim 1. Wei et al contact these yeast with plasmids encoding PMR1 with a library of mutations (see p. 23928, col. 2, for example). Wei et al measure the growth characteristics of yeasts harboring mutant pmr1p, a readout of manganese transport (see p. 23928, col. 2, para 1; see fig. 1, p. 23929, as examples). In one experiment, the assays are carried out using isolated golgi membranes, reading on claim 2 (see Experimental Procedures, "$^{45}Ca^{2+}$ Transport Assays, p. 23928, col. 1; see p. 2391, col. 1 and Fig. 5, as examples). They report that they can observe ^{54}Mn transport variations into Golgi membranes in Pmr1 mutants (see p. 23931, col. 1, for example). As is known in the art, yeast cells are eukaryotic cells, reading on claims 3, 4, 6, and 7. The use of pmr1p in this paper reads on claims 10 and 11. Wei et al demonstrate that one mutation in Pmr1 results in a transporter with selectivity for Ca^{2+} only, and manganese transport is abolished, reading on instant claim 12 (see p. 23931, col. 1, for example). Pmr1p is a transporter that can transport Mn^{2+} cations into the secretory pathway; a mutant reads on an agent that inhibits manganese ion transport out of a cell as recited in claim 13 (see p. 23928, col. 1, para 1, for example). Lastly, as stated above, Wei et al report that manganese transport can be measured using ^{54}Mn, reading on claim 16.

Therefore it is deemed that the teachings of Wei et al anticipate instant claims 1-4, 6, 7, and 10-16.

Claims 1, 3-6, 8-10, 14, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Aussel et al (Biochem J, 1996) in light of Poulsen et al (Biochem J, 1995) and Van Balen et al (Biochem Biophys Acta, 2004). Aussel et al teach a method of inhibiting the divalent cation transport with La^{3+}. La^{3+} can also be used to block Mn^{2+} transport (see p. 911, col. 2; see Fig. 4, p. 912, as examples). The experiments are performed using Jurkat cells, an immortalized lymphocyte cell line, reading on claims 1, 3-6, 8, and 9. The intracellular store of Ca^{2+} is increased from both the exterior of the cell and the endoplasmic reticulum when the cell is exposed to either a CD3 monoclonal antibody or the compound thapsigargin. Mn^{2+} acts analogously, and is used in studies as a surrogate for Ca^{2+}. Aussel et al teach that Mn^{2+} intracellular concentration is increased by addition of CD3 mAb or thapsigargin, and the increase is inhibited by the addition of La^{3+} (see p. 910, col. 2; see p. 911, col. 2; see Fig. 4, p. 912, as examples). Poulsen et al teach that thapsigargin is a highly selective inhibitor of SERCA (see Abstract, p. 749, for example). Van Baelen et al teach that SERCA is a P-type ATPase (see p. 104, col. 2, for example).

Therefore the teachings of Aussel et al are deemed to anticipate instant claims 1, 3-6, 8-10, 14, and 15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6, 8-10, and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aussel et al (Biochem J, 1996) in view of Weed et al (J General Physiol, 1960).

The teachings of Aussel et al are discussed above and applied as before.

Aussel et al do not teach that one should use radiometric or polarographic methods to measure Mn^{2+} transport.

Weed et al teach the measurement of Mn^{2+} transport across the membrane of red blood cells. They teach that one can use ^{54}Mn to detect manganese transport, and point out that ^{54}Mn is an easily used isotope for radiometric detection, because it has broad enzyme specificity and a long half-life (see p. 302, for example). They also teach that Mn^{2+} can be measured in solutions by polarographic methods, and they correlate well with measurements taken by radiometric methods (see p. 304 last para to p. 305, first para).

A person of ordinary skill in the art at the time the invention was made would have been motivated to measure manganese transport with a radiometric method or a polarographic method because Weed et al teach that in particular radiometric methods

are easily performed because Mn^{2+} has a long half life, and polarographic methods in general correlate well with radiometric methods.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to measure manganese transport in yeast cells by radiometrically measuring manganese isotope uptake into yeast cells, or measure the manganese concentration in solutions by a polarographic method.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clark D. Petersen whose telephone number is (571)272-5358. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571)272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CDP
6/7/2007

Jon Weber
Supervisory Patent Examiner